abscess reported in the literature have been treated by abdominal hysterectomy, salpingo-oophorectomy and, in addition, administration of penicillin or a cephalosporin (Table 1, patient 5). The mode of administration and the dose of penicillin given have varied widely. The smallest dose of penicillin given to any patient was 1 gram per day of penicillin V for three months; this patient was reported to be well seven months after therapy began.[3] It is noteworthy that one patient with tubo-ovarian actinomycosis secondary to appendicitis was treated with a total of 86.8 million units of penicillin over approximately three months and a total of 9.5 grams of sulfadiazine, and subsequently had a normal pregnancy and delivery.[12] Data derived from in vitro sensitivity testing as well as treatment of actinomycosis in other sites[19-21] provide evidence that erythromycin, tetracyclines and clindamycin, as well as cephalothin and chloramphenicol, are reasonable alternative drugs for treatment of tubo-ovarian actinomycosis in patients who are allergic to penicillin.

Summary

Tubo-ovarian actinomycosis was diagnosed in a woman who had been using an IUD. The organism was identified by histologic analysis and culture. This case and 20 previously reported cases of IUD-associated pelvic actinomycosis are reviewed. Methods of diagnosis and management are emphasized because this infection is more likely to occur in view of the increasing use of IUD's.

REFERENCES

1. Brown JR: Human actinomycosis—A study of 181 subjects. Human Pathol 4:319-330, Sep 1973

2. Brenner RW, Gehring SW: Pelvic actinomycosis in the presence of an endocervical contraceptive device—Report of a case. Obstet Gynecol 29:71-73, Jan 1967

3. Dische FE, Burt LJ, Davidson NJ, et al: Tubo-ovarian actinomycosis associated with intrauterine contraceptive devices. J Obstet Gynecol Br Commonw 81:724-729, Sep 1974

4. Henderson SR: Pelvic actinomycosis associated with an intrauterine device. Obstet Gynecol 41:726-732, May 1973

5. Lomax CW, Harbert GM Jr, Thornton WN Jr: Actinomycosis of the female genital tract. Obstet Gynecol 48:341-346, Sep 1976

6. McCormick JF, Scorgie RDF: Unilateral tubo-ovarian actinomycosis in the presence of an intrauterine device. Am J Clin Pathol 68:622-626, Nov 1977

7. Purdie DW, Carty MJ, McLeod TIF: Tubo-ovarian actinomycosis and the IUCD. Br Med J 4:1392, Nov 1977

8. Schiffer MA, Elguezabal A, Sultana M, et al: Actinomycosis infections associated with intrauterine contraceptive devices. Obstet Gynecol 45:67-72, Jan 1975

9. Seligman PA, Plaut ME, Lippes J, et al: Tubo-ovarian actinomycosis. NY State J Med 76:278-280, Feb 1976

10. Surur F: Actinomycosis of female genital tract. NY State J Med 74:408-411, Feb 1974

11. Paalman RJ, Dockerty MB, Mussey RD: Actinomycosis of the ovaries and fallopian tubes. Am J Obstet Gynecol 48:419-431, Sep 1949

12. Richter GO, Pratt JH, Nichols DR, et al: Actinomycosis of the female genital organs. Minnesota Med 55:1003-1006, Nov 1972

13. Harvey JC, Cantrell JR, Fisher AM: Actinomycosis—Its recognition and treatment. Ann Intern Med 46:868-885, May 1957

14. Gupta PK, Hollander DH, Frost JK: Actinomycetes in cervico-vaginal smears—An association with IUD usage. Acta Cytol (Baltimore) 20:295-297, Jul-Aug 1976

15. Graybill JR, Silverman BD: Sulfur granules—Second thoughts. Arch Intern Med 123:430-432, Apr 1969

16. Holmberg K, Nord CE, Wadström T: Serological studies of *Actinomyces israelii* by crossed immunoelectrophoresis—Taxonomic and diagnostic applications. Infect Immun 12:398-403, Aug 1975

17. Hotchi M, Schwarz J: Characterization of actinomycotic granules by architecture and staining methods. Arch Pathol 93: 392-400, May 1972

18. Bhagavan BS, Gupta PK: Genital actinomycosis and intrauterine contraceptive devices. Human Pathol 9:567-578, Sep 1978

19. Lerner PI: Susceptibility of pathogenic actinomycetes to antimicrobial compounds. Antimicrob Agents Chemother 5:302-309, Mar 1974

20. Herrell WE, Balows A, Dailey JS: Erythromycin in treatment of actinomycosis. Antibiot Med 1:507-512, Sep 1955

21. Weese WC, Smith IM: A study of 57 cases of actinomycosis over a 36-year period—A diagnostic "failure" with good prognosis after treatment. Arch Intern Med 135:1562-1568, Dec 1975

Refer to: Williams GF, Calin A, Gospe SR, et al: Post-*Yersina* arthritis. West J Med 132:535-539, Jun 1980

Post-*Yersinia* Arthritis

GORDON F. WILLIAMS, MD
ANDREI CALIN, MD
Palo Alto, California

STEPHEN R. GOSPE, MD
Santa Rosa, California

JOHN J. MILLER, III, MD, PhD
Palo Alto, California

REACTIVE ARTHRITIS is the term used at present for a sterile arthritis following infection in a part of the body that is remote from the joints.[1-4] Reiter syndrome is an example. The arthritis is usually of abrupt onset, involves relatively few joints and, characteristically, occurs after a latent period of a few days to two or three weeks. The antecedent infections are bacterial or chlamydial. By custom, the term excludes viral-associated arthritides. This report describes the cases of four patients in Northern California with arthritis following gastroenteritis caused by *Yersinia enterocolitica*. This syndrome was first described by Ahvonen and colleagues[1] in a report of 11 patients in Finland with erythema nodosum, including arthritis in two patients, following *Yersinia* enteritis. A similar syndrome may be associated

From Children's Hospital at Stanford; the Department of Pediatrics, Division of Rheumatology, and the Department of Medicine, Division of Immunology, Stanford University School of Medicine.

Submitted, revised, July 30, 1979.

Reprint requests to G. F. Williams, MD, Children's Hospital at Stanford, 520 Willow Road, Palo Alto, CA 94304.

ABBREVIATIONS USED IN TEXT

ANA = antinuclear antibody
ESR = erythrocyte sedimentation rate
LF = latex fixation
PMN = polymorphonuclear

with diarrheal disease due to *Salmonella*[2] or *Shigella*.[3] Aho and associates[4] noted the presence of the HLA-B27 histocompatibility antigen in 43 of 49 patients with reactive arthritis following *Yersinia* infection, as compared with 3 of 20 patients who had *Yersinia* enteritis without arthritis. In the normal Finnish population the prevalence of the HLA-B27 antigen is 14 percent. Studies of patients with reactive arthritis following *Salmonella*[5] and *Shigella*[3] infections have shown the same relationship to the HLA-B27 antigen.

Reports of Cases

CASE 1. In an 11-year-old girl from a dairy farm in Sonoma County, California, diarrhea developed in October 1977; it lasted for ten days and was never bloody. She lost 10 pounds. No enteric bacterial pathogens were recovered on stool culture, and one stool examination was negative for ova and parasites. Twelve days following the onset of diarrhea, pain in one hip developed, sufficient to make her limp. Two days later swelling and pain developed in the right wrist, followed within a few hours by pain and swelling of both ankles and over the dorsal surfaces of both feet. No other abnormalities were present on physical examination, and the girl remained afebrile. The leukocyte count was 12,400 per cu mm, with a differential of 71 percent polymorphonuclear (PMN) leukocytes, 2 percent banded forms, 20 percent lymphocytes, 5 percent monocytes, 1 percent eosinophils and 1 percent basophils. Hemoglobin was 11.8 grams per dl and the hematocrit was 33.9 percent. The erythrocyte sedimentation rate (ESR) was 58 mm per hour. The platelet count was 690,000 per cu mm. Findings of the latex fixation (LF) and antinuclear antibody (ANA) tests, analysis of the urine and a test for the hepatitis B surface antigen (HBsAg) were all negative. There were no significant titers of antibodies against *Salmonella* somatic antigen of types A, B, D or E, or against *Brucella*. The test for HLA-B27 antigen was positive, and a serologic titer for antibodies against the intestinal pathogen *Yersinia enterocolitica* (type 21 antigen) was positive in a dilution of 1:320. Treatment with acetylsalicylic acid, 0.6 gram four times per day, was begun, and later the dosage was increased to 0.9 gram four times per day. On this latter dosage, with a salicylate level of 29 mg per dl, the serum glutamic oxaloacetic transaminase (SGOT) level reached 143 IU per liter. The acetylsalicylic acid dosage was reduced to 0.6 gram three times a day. The arthritis improved gradually, but progressively, over six months, and she has remained asymptomatic since that time. In this case there has never been clinical or roentgenographic evidence of sacroiliitis.

CASE 2. A 13-year-old boy from Santa Clara County, California, vacationed with his family on the Sacramento River Delta in August 1978, where he swam in the river and drank well water and milk from local dairy farms. On September 10, 1978, fever, sore throat and slight cramps developed in the boy. A throat culture was negative for *Streptococcus,* and he improved in two or three days. On October 4 a high temperature, to 39.4°C (103°F), recurred and lasted for five weeks. The fever was accompanied by nonbloody diarrhea with up to eight stools per day. This continued for four days, and was followed by pain in the boy's thighs, ankles and the right hip. Only a moderate conjunctivitis was found on physical examination. Pain occurred in the left hip the next day, but all pain improved with treatment with acetylsalicylic acid, in a dosage of 0.6 gram, three times a day. The complete blood count showed no abnormalities, other than a minimal leukocytosis with a slight increase in banded polymorphonuclear leukocytes. The ESR was 56 mm per hour; the antistreptolysin titer was 125 Todd units and the LF and ANA tests were negative. A tine test and a coccidioidin skin test were both negative as well. On the tenth day of fever, and five days after diarrhea had ceased, an erythematous, indurated rash "consistent with erythema nodosum," appeared on his lower legs. Acetylsalicylic acid therapy was discontinued; the rash lasted less than 48 hours and never reappeared. As the rash was fading, pain in the left sacroiliac joint developed. However, on physical examination, no abnormalities were noted.

During the second week arthralgia of the right temporomandibular joint and the right wrist occurred. During the third week of fever, a repeat complete blood count again showed no abnormalities other than an increased number of band-form PMN's. The ESR was 58 mm per hour. The test for HLA-B27 was positive. Objective evi-

dence of arthritis first became apparent at this time, with tenderness over the right temporomandibular and left sacroiliac joints. Radiographs of these joints gave normal findings. Again, a complete blood count and an analysis of the urine were within normal limits and the ESR increased. Two blood cultures were sterile; a urine culture grew 400 colonies of mixed flora, a stool culture grew normal enteric flora. Antibodies against *Y enterocolitica* were found in titers of 1:320 (type 14 antigen) and 1:160 (type 7 antigen). Agglutinating, hemagglutinating or complement-fixing titers against *Coccidioides,* typhoid O, typhoid H, *Proteus* strains OX2, OXK, and OX19, *Brucella,* influenza A, influenza B, adenovirus, *Mycoplasma pneumoniae,* Q fever, and respiratory syncytial (RS) virus were all within normal ranges.

Fever continued, unless controlled by acetylsalicylic acid, for the next 20 days, with temperatures as high as 39.4°C (103°F). After 17 days persistent pain and swelling of the right elbow, the right ankle and the proximal interphalangeal joint of the right fifth finger developed. Two days later pain, tenderness, limitation of motion in the right shoulder and severe pain with limitation of motion of the left hip occurred. Subsequently, pain in both heels and on the plantar surfaces of his feet when walking, a right knee effusion, and swelling of the left ankle also developed. The boy was severely disabled until treatment with indomethacin was started. There was dramatic improvement within 24 hours with a dosage of 25 mg two times a day. Improvement continued progressively, with gradual recession of joint swelling over the next six weeks, after which he was able to run, play vigorous games and ride his bicycle. However, treatment with indomethacin in dosages as high as 25 mg four times a day was still needed to control polyarthralgia, foot pain and effusion of the right knee four months after onset. Symptoms or signs of urethritis were never present.

CASE 3. A 36-year-old man from Sonoma County, California, was first seen by one of us (S.R.G.) two months following the onset of an illness that began in mid-November 1977. The patient described his condition as a "stomach upset" and diarrhea that lasted three to four days. At about the time that the diarrhea subsided, swelling of the right knee developed, soon followed by swelling of the left knee, left ankle and the left forefoot. Because multiple joint swelling had persisted for three to four weeks without improvement, the patient consulted his own physician who started treatment with phenylbutazone, 100 mg three times a day. A physical examination on January 21, 1978, disclosed swelling and tenderness of the left ankle, particularly over the medial malleolus, together with minimal swelling, tenderness and pain on movement of the second and third metatarsophalangeal joints of the left foot and the metatarsophalangeal joints of both great toes. There was questionable swelling of both knees. A complete blood count and analysis of the urine showed no abnormalities. The ESR was 49 mm per hour; LF and ANA tests were negative. The test for HLA-B27 antigen was positive. Sera for antibodies against *Y enterocolitica* were obtained on July 24 and August 24; they were positive in titers of 1:160 and 1:80 respectively, against the type 7 antigen. X-ray films of the knees, feet and pelvis disclosed no abnormalities. The patient's condition improved slowly through the summer of 1978; when last seen on September 12, 1978, he had only minimal symptoms of pain in the feet, easily controlled with small doses of acetylsalicylic acid. When queried by telephone on January 15, 1979, he reported that he had been entirely asymptomatic for two or three months.

CASE 4. A 35-year-old woman from Santa Clara County, California, noted the onset of pharyngitis, diarrhea, abdominal distension and fever following a visit to Washington state. The diarrhea lasted ten days, with mucus but no blood. Two weeks after the onset of diarrhea, pain and swelling of the left knee, and low back pain in association with fever developed. There was minimal dysuria and difficulty of micturition. The syndrome slowly remitted over the next six months. During the early stages of the illness she lost 20 pounds. She has not had symptoms of eye disease or any other symptoms. Some 24 months following the onset of the illness she has minimal back pain and discomfort in the left knee.

Tests were negative for LF and ANA, but positive for the HLA-B27 antigen. At the onset of the arthritis, the ESR was 58 mm per hour; the hematocrit was 30.8 percent and the results of SMA-12 panel tests were within normal limits. Stool examinations for ova, parasites and other pathogens were negative. Analysis of synovial fluid from the left knee showed a leukocyte count of 9,000 per cu mm, with 48 percent neutrophils and 30 percent lymphocytes. A synovial fluid LF test was negative. No crystals were seen. Serum

TABLE 1.—*Clinical and Laboratory Data for Four Patients With Post-*Yersinia *Arthritis*

Patient	*1*	*2*	*3*	*4*
Age (years)/sex	11/F	13/M	36/M	35/F
Duration of diarrhea (days)	10	4	4	10
Fever	−	+	−	+
Back pain	−	+	−	+
Latent period before onset of arthritis (days)	12	4	4	14
Erythema nodosum	−	+	−	−
Arthritis	+	+	+	+
Conjunctivitis	−	+	−	−
Urethritis	−	−	−	+
Erythrocyte sedimentation rate (mm per hour)	58	56	49	58
Yersinia agglutination titer	1:320	1:320	1:160*	1:80*
HLA-B27 antigen	+	+	+	+
Duration of arthritis (month)	6	4+	12	6

*Specimens submitted for agglutination titers late in the course of the disease.

specimens were obtained four and eight weeks after the onset, and a titer of 1:80 was found for *Y enterocolitica* type 4 antigen on both occasions. Antibody to *Salmonella* was not present.

Discussion

Most of the reports of reactive arthritis following *Yersinia* infection have been from the Scandinavian countries, principally from Finland, where the condition was first described.[1] *Yersinia* infection is known to occur in North America,[6-11] but there have been only a few reports of reactive arthritis following this infection in this continent.[6,8,9] *Y enterocolitica* has recently been reported[12] to be the second most common cause of bacterial gastroenteritis in the Montreal area. No data regarding the incidence of *Yersinia* infection in the United States are known to us. Our experience suggests that *Yersinia* infection may be a more common cause of reactive arthritis or of Reiter syndrome in the United States than hitherto recognized.

Y enterocolitica is difficult to identify as the significant pathogen in stool cultures as they are usually carried out.[11] The growth characteristics and requirements of *Y enterocolitica* have been described by Sonnenwirth.[13] This species of organism grows more slowly at 35° to 37°C than other intestinal pathogens. Stool cultures should be incubated for at least two days before being discarded as negative. Overgrowth of other organisms may occur. Growth and identification of *Y enterocolitica* are greatly dependent on temperature. Identifying tests may be positive at 22° and 25°C, but negative (or delayed) at 37°C. Isolation can be aided by keeping stool specimens at 4°C for one to two days before culture. Thus, *Yersinia* may be overlooked in a stool culture done in a laboratory if a technician is oriented primarily toward detecting *Salmonella, Shigella* or enteropathogenic *Escherichia coli* in cases of infectious diarrhea.

Serologic studies may document infection where stool cultures have not. In a careful study of 60 patients seen over two years in Finland, Leino and Kalliomaki[14] depended largely on elevated antibody titers to establish the diagnosis in patients who presented with findings of fever, diarrhea, abdominal pain, erythema nodosum and arthritis to suggest yersiniosis. In their patients, the lowest significant titer was 1:160. Ahvonen,[15] in a serologic study of 334 cases that fulfilled clinical and laboratory criteria for the diagnosis of *Yersinia* infection, reported that the titer usually attained its maximum value after one or two weeks of illness, and then gradually declined. A significant drop in titer had usually occurred within two months, but was sometimes delayed. Ahvonen also carried out a study involving 1,580 Finnish blood donors, finding only 4 (0.25 percent) persons with *Yersinia* titers of 1:160 or greater. In this study, there were 56 persons (3.5 percent) with titers of 1:40 or 1:80. We know of no similar studies having been done in the United States.

Paired antibody determinations should be done to establish clearly that *Yersinia* organisms are the significant infectious agent in cases where it is not possible to recover organisms by stool culture. The first specimen should be drawn as early as possible in the course of the illness, and the second four to six weeks later. A titer of 1:160 or greater in at least one of these will suffice to support a diagnosis of *Yersinia* infection. Usually, the highest titer can be expected in the first specimen, with a fall of one tube dilution or greater in the second. Because we failed to obtain paired specimens in cases 1 and 2, and obtained paired serologic studies late in cases 3 and 4, the condition of the patients we report here can most accurately be identified as "possible post-*Yersinia* arthritis." In case 4, where the titers, in specimens obtained four and eight weeks after onset, were both 1:80, the minimum criterion of a 1:160 titer was not observed. We report this case because illness of the sort that occurred, in a patient with the HLA-B27 phenotype, should strongly

suggest either yersiniosis or post-*Salmonella* or post-*Shigella* arthritis. Failure to show a significant titer at four and eight weeks after onset underscores the importance of obtaining the first serologic specimen early in the course of illness. (Serologic studies reported here were carried out by the Microbial Diseases Laboratory of the State of California, Department of Health, 2151 Berkeley Way, Berkeley, CA 94704.)

Table 1 presents similarities and differences in clinical and laboratory data for the four cases reported here.

Conclusion

The four cases reported show that reactive arthritis following enteritis due to *Y enterocolitica* may occur in persons residing in Northern California, a syndrome previously reported most frequently in Scandinavia. Because reactive arthritis is known to occur with greatest frequency in persons who are HLA-B27 positive, a test for this antigen should be done in patients in whom arthritis in association with a febrile or diarrheal disease has developed, particularly if *Yersinia, Salmonella* or *Shigella* infection is suspected or proved. At this time the prognosis for these patients is not known. It had been thought that this syndrome was always self-limited, but Calin and Fries[3] have found some patients with prolonged and persistent arthritis following diarrheal disease due to *Shigella.*

REFERENCES

1. Ahvonen P, Sievers K, Aho K: Arthritis associated with *Yersinia enterocolitica* infection. Acta Rheumatol Scand 15:232-253, 1969
2. Warren CPW: Arthritis associated with *Salmonella* infections. Ann Rheumat Dis 29:483-487, 1970
3. Calin A, Fries JF: An "experimental" epidemic of Reiter's syndrome revisited—Follow-up evidence on genetic and environmental factors. Ann Intern Med 84:564-566, 1976
4. Aho K, Ahvonen P, Lassus A, et al: HL-A27 in reactive arthritis—A study of Yersinia-arthritis and Reiter's disease. Arthritis Rheum 17:521-526, 1974
5. Friis J, Svejgaard A: Salmonella arthritis and HL-A27 (Letter). Lancet 1:1350, 1974
6. Chalmers A, Kaprove RE, Reynolds WJ, et al: Postdiarrheal arthropathy of *Yersinia pseudotuberculosis.* Can Med Assoc J 118: 515-516, 1978
7. Gutman LT, et al: An inter-familial outbreak of *Yersinia enterocolitica* enteritis. N Engl J Med 288:1372-1377, 1973
8. Ford DK, Henderson E, Price GE, et al: Yersinia-related arthritis in the Pacific Northwest. Arthritis Rheum 20:1226-1230, 1977
9. Jacobs JJ: *Yersinia enterocolitica* arthritis. Pediatrics 55:236-238, 1975
10. Sonnenwirth AC, Weaver RE: *Yersinia enterocolitica* (Letter). N Engl J Med 283:1468, 1970
11. Kohl S, Jacobson JA, Nahmias A: *Yersinia enterocolitica* infections in children. J Pediatr 89:77-79, 1976
12. Marks MI, Pai CH, Lafleur L, et al: *Yersinia enterocolitica* gastroenteritis in children (Abstract). Pediatr Res 12:496, 1978
13. Sonnenwirth AC: Yersinia, *In* Lennette EC, Spaulding EH, Truant JP (Eds): Manual of Clinical Microbiology, 2nd Ed. Washington, DC, Society of Microbiology, 1974, pp 222-230
14. Leino R, Kalliomaki JL: Yersiniosis as an internal disease. Ann Intern Med 81:458-461, 1974
15. Ahvonen P: Human yersiniosis in Finland—I. Bacteriology and serology. Ann Clin Res 4:30-33, 1972

Refer to: Jung RC, Aaronson J: Death following inhalation of mercury vapor at home. West J Med 132:539-543, Jun 1980

Death Following Inhalation of Mercury Vapor at Home

RALPH C. JUNG, MD
JEFFREY AARONSON, MD
Los Angeles

THE INHALATION of toxic fumes and metallic vapors is a fairly common occurrence in industry. There are ample accounts describing the effects from the inhalation of vaporized mercury on the respiratory tract and other organ systems.[1-5] Ramazzini[6] in 1940 gave one of the earliest descriptions of the consequences of such exposure. Studies indicate that members of the dental profession and workers in the fur or felt hat-making industry have been at greatest risk for exposure to mercury.[2] Other industrial exposures have occurred primarily when metallic mercury has been accidentally vaporized in a high-temperature environment.[3-5]

Fortunately, deaths among adults exposed in industry have been very rare.[4] In contrast, accidental exposure to mercury has resulted in deaths among children and has caused chronic disability in adults. In the following report we discuss what appears to be the first death of an adult exposed to mercury vapor in the home. We have included hemodynamic measurements, which have not been described previously in these patients.

Report of a Case

A 53-year-old man, suffering from severe respiratory distress, was transferred to the Los Angeles County/University of Southern California Medical Center for specialized renal and respiratory care. He had been in good health until approximately two weeks before admission. At that time, while the patient was working with elemental mercury in an ore distillation process on his kitchen stove, chills, fever, dyspnea, headache,

From the Pulmonary Disease Service, Department of Medicine, University of Southern California School of Medicine and Los Angeles County/USC Medical Center, Los Angeles.

Submitted July 16, 1979.

Reprint requests to: Ralph C. Jung, MD, Rm 11-840, LAC-USC Medical Center, 1200 N. State Street, Los Angeles, CA 90033.